Abstract:

Background: Clinical and experimental data demonstrating that excess aldosterone and insulin interact at target tissues. It has been shown that increased levels of aldosterone contribute to the development of insulin resistance/type-2 diabetes. However, the molecular mechanisms and the relationship among aldosterone, glucose metabolism, and insulin resistance have not been clarified so far. *Objective*: To identify the dose-dependent effects of aldosterone on the expression of insulin signaling molecules (insulin receptor, insulin receptor substrate-1 & 2, β-arrestin-2, c-Src, Akt, AS160, GLUT4 & 2) and free radical generation & lipid peroxidation in gastrocnemius muscle and liver of adult male rat. *Result:* Excess aldosterone caused glucose intolerance in a dose-dependent manner. Serum insulin and aldosterone were significantly increased, whereas serum testosterone was decreased. Aldosterone treatment impaired the rate of glucose uptake, oxidation, and insulin signal transduction in the gastrocnemius muscle and liver through defective expression of IR, IRS-1, Akt, and GLUT4 & 2 genes. Phosphorylation of IRS-1 and Akt was also reduced in a dose-dependent manner. *Conclusion:* Excess aldosterone results in glucose intolerance as a result of impaired insulin signal transduction and the associated decrease in glucose uptake and oxidation in skeletal muscle and liver. Elevated fasting blood glucose and its association with increased circulating level of insulin is suggestive of insulin resistance. In addition to this, it is inferred that excess aldosterone may act as one of the causative factors for the development of insulin resistance and thus increased incidence of type-2 diabetes.